A systematic review and meta-analysis: probiotics in the treatment of irritable bowel syndrome


CRD summary
The authors concluded that probiotics may alleviate some symptoms of irritable bowel syndrome after several weeks of treatment. Longer-term studies were needed, focused on the type and optimal dose of probiotics and on subgroups of patients who may benefit. The review was well conducted and the conclusions appear reliable.

Authors’ objectives
To determine whether probiotics alleviate the symptoms of irritable bowel syndrome.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Database of Systematic Reviews, AMED and Cochrane Central Register of Controlled Trials were searched. A high-sensitivity filter was used in the EMBASE search. Search dates varied and spanned 1950 to August 2007. Search terms were reported. Current Controlled Trials was searched for ongoing studies. Attempts were made to contact their lead researchers. The reference lists of retrieved articles were handsearched. The search was limited to studies in English.

Study selection
Randomised placebo-controlled trials of any probiotic therapy were eligible for inclusion, provided participants were adults or children with irritable bowel syndrome consistent with Manning or Rome diagnostic criteria. The two study groups were required to receive the same treatment apart from provision of probiotics to one group. The primary review outcome was improvement in overall symptoms (pain, flatulence, bloating, anxiety and quality of life). Secondary outcomes were improvement in individual symptoms.

Most studies included both men and women; most participants in the review were female. Participant ages ranged from six to 78 years; only two studies included children. In most cases, Manning or Rome diagnostic criteria were used. Some studies were restricted to participants with specific irritable bowel syndrome symptoms. Probiotics regimens varied widely in type of organism, dose and strength, and some studies used a combination of several probiotics. Some studies had more than one intervention arm. Duration of treatment varied from four weeks to six months. The definition of overall symptoms varied across studies and a variety of differing scales was used to measure for continuous outcomes. Most of the included studies were conducted in Europe or USA.

Two reviewers independently selected articles for inclusion.

Assessment of study quality
Up to four points in total were allocated for the following aspects of study validity: randomisation method; allocation concealment; blinding; and intention to treat analysis. Two reviewers independently assessed study validity, with disagreements resolved by discussion.

Data extraction
Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the numbers of events in each arm of each study. Mean differences between the groups were calculated for continuous outcomes, with 95% CIs. The most conservative estimate was used for studies with more than one intervention arm.

Two reviewers independently extracted data. Disagreements were resolved by discussion. Study authors were contacted to request missing data.

Methods of synthesis
Dichotomous data were combined to calculate pooled ORs using a Mantel-Haenszel fixed-effect model and continuous data were combined to calculate standardised mean differences (SMDs), both with 95% CIs. Heterogeneity was assessed using the $I^2$ statistic. Publication bias was assessed by means of a funnel plot. The number needed to treat for improvement in one patient was calculated for the primary outcome. A sensitivity analysis was conducted to assess the impact of differences between the studies in quality score (4 versus <4). A subgroup analysis examined the differential effects in children and adults. There were insufficient data to subgroup studies by type of probiotic.

**Results of the review**

Fourteen RCTs were included (n>1,125, range 24 to 362 where stated). Quality varied: four studies scored a maximum 4 points, but seven scored 2 or less.

**Overall improvement:** There was a modest but statistically significant improvement in the probiotics group versus placebo after several weeks of treatment, without significant heterogeneity: OR 1.6 (95% CI 1.2 to 2.2, $I^2=28%$; seven RCTs, n=895); SMD 0.23 (95% CI 0.07 to 0.38, $I^2=0%$, six RCTs, n=657). The number needed to treat was approximately one to 21. Analysis of adults-only data did not change the statistical significance of the results. Sensitivity analysis by study quality materially altered the findings. Assessment for publication bias was inconclusive.

**Individual symptoms:** Dichotomous data showed statistically significant improvement in the probiotics group versus placebo in abdominal pain (OR 2.88, 95% CI 1.84 to 4.50, $I^2=24%$; seven RCTs, n=398). Analysis of adults-only data did not change the statistical significance of the results. Dichotomous data showed statistically significant improvement in the probiotics group versus placebo in flatulence (OR 2.31, 95% CI 1.37 to 3.9, $I^2=7%$) and bloating (OR 1.75, 95% CI 1.03 to 2.96, $I^2=0%$; four RCTs, n=253). However, continuous data (nine, five and four RCTs) showed no statistically significant difference between probiotics and placebo for these outcomes, with high heterogeneity for analyses of abdominal pain ($I^2=51%$) and flatulence ($I^2=49%$). Data on quality of life were unsuitable for pooling: three of four relevant RCTs found no statistically significant difference between probiotics and placebo.

**Adverse effects:** None of the 14 RCTs that measured this outcome reported statistically significant findings.

Other results were reported in the review.

**Authors' conclusions**

Probiotics may alleviate some of the symptoms of irritable bowel syndrome after several weeks of treatment. Longer-term studies were needed, these should focus on the type and optimal dose of probiotics and on subgroups of patients who may benefit.

**CRD commentary**

The objectives and inclusion criteria of the review were clear. Relevant sources were searched for published and unpublished studies, although the restriction to studies in English meant that the review may have been prone to language bias. Steps were taken to minimise reviewer bias and error by having more than one reviewer independently undertake study selection, validity assessment and data extraction. Appropriate validity criteria were used and study quality was taken into account in the interpretation of findings. Appropriate statistical techniques were used to combine studies and assess for heterogeneity, and the risk of publication bias was assessed. Potential reasons for the inconsistencies between dichotomous and continuous data were suggested (such as use of differing scales). In view of these inconsistencies, the authors’ conclusions were suitably cautious. The review was well conducted and the authors’ conclusions appear reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that longer-term studies on probiotics for irritable bowel syndrome were required. Individual symptoms of irritable bowel syndrome, including urgency and difficult defecation, should be measured as outcomes and adverse events should be clearly reported. Studies should be focused on the type and optimal dose of probiotics and identify which groups of patients were most likely to benefit.
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.